

§ Appl. No. 09/889,227  
Amdt. dated October 25, 2006  
Reply to Office Action of, May 25, 2006

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Currently Amended) A compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is  $-\text{NH}-\text{C}(\text{O})-\text{NH}-$ ,

A is a substituted moiety of the formula:



wherein L is phenyl, optionally substituted by halogen, up to per-halo, and  $\text{W}_n$ , where n is 0-3;

wherein each W is independently selected from the group consisting of  $\text{C}_1$ - $\text{C}_5$  linear or branched alkyl,  $\text{C}_1$ - $\text{C}_5$  linear or branched haloalkyl up to perhaloalkyl and  $\text{C}_1$ - $\text{C}_3$  alkoxy  $\text{L}^1$  is selected from pyridinyl substituted by  $-\text{C}(\text{O})\text{R}_x$ , and

optionally substituted with 1-3 additional substituents independently selected from the group consisting of  $\text{R}^7$  and halogen;

wherein  $\text{R}_x$  is  $\text{NR}_a\text{R}_b$  and  $\text{R}_a$  and  $\text{R}_b$  are

A) independently

- a) hydrogen,
- b)  $\text{C}_1$ - $\text{C}_{10}$  alkyl,
- c)  $\text{C}_6$  aryl,
- d) pyridinyl
- e) substituted  $\text{C}_{1-10}$  alkyl,

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- f) substituted C<sub>6</sub> aryl,
  - g) substituted pyridinyl
  - h) -phenylpiperazine(pyridinyl),
  - i) -phenylmorpholinyl,
  - j) -ethylmorpholinyl,
  - k) -ethylpiperidyl,
  - l) -methyl pyrrolidinyl,
  - m) -methyl tetrahydrofuryl,
- or
- n) -C<sub>2</sub>H<sub>4</sub>NH(phenyl);

where when R<sub>a</sub> and R<sub>b</sub> are a substituted group, they are substituted by

- a) halogen up to per halo,
  - b) hydroxy,
  - c) -N(CH<sub>3</sub>)<sub>2</sub>,
  - d) C<sub>1</sub>-C<sub>10</sub> alkyl,
  - e) C<sub>1</sub>-C<sub>10</sub> alkoxy,
  - f) halosubstituted C<sub>1-6</sub> alkyl, or
  - g) -OSi(Pr-i)<sub>3</sub>; or
- B) R<sub>a</sub> and R<sub>b</sub> together form piperazine or a substituted piperazine with substituents selected from the group consisting of
- a) halogen,
  - b) hydroxy,
  - c) C<sub>1-10</sub> alkyl,
  - d) pyridinyl
  - e) C<sub>1-10</sub> alkoxy,

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- f) C<sub>6</sub> aryl,
- h) g) halo substituted C<sub>6</sub> aryl, and
- i) h) N-(4-acetylphenyl);

M is selected from the group consisting of oxygen and sulfur;

and

B is

phenyl, substituted with 1-3 substituents independently selected from the group consisting of halogen and R<sup>7</sup>,

and R<sup>7</sup> is

- (a) C<sub>1</sub>-C<sub>6</sub> linear or branched alkyl, optionally substituted with 1-3 halogen substituents; or
- (b) C<sub>1</sub>-C<sub>6</sub> linear or branched alkoxy.

2. **(Canceled)**

3. **(Previously Presented)** A compound as in claim 1 wherein M is oxygen .

4. **(Previously Presented)** A compound as in claim 1 wherein the cyclic structures of B and L bound directly to D are substituted in the ortho position by hydrogen.

5. **(Canceled)**

6. **(Currently Amended)** A compound of claim 1 wherein B of Formula I is phenyl, substituted with 1-3 substituents independently selected from the group consisting of ~~halogen~~ chlorine, C<sub>1</sub>-C<sub>6</sub> alkoxy or up to per halo substituted C<sub>1</sub>-C<sub>6</sub> alkyl.

7. **(Currently Amended)** A compound of claim 3 wherein B of Formula I is

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phenyl, substituted with 1-3 substituents independently selected from the group consisting of ~~halogen~~  
chlorine, C<sub>1</sub>-C<sub>6</sub> alkoxy, or substituted C<sub>1</sub>-C<sub>6</sub> alkyl, substituted by one or more halogen substituents.

**8. (Currently Amended)** A compound of claim 4 wherein B of Formula I is phenyl, substituted 1 to 3 times by 1 or more substituents selected from the group consisting of ~~halogen~~  
chlorine, C<sub>1</sub>-C<sub>6</sub> alkoxy or up to per halo substituted C<sub>1</sub>-C<sub>6</sub> alkyl.

**9. (Previously Presented)** A compound of claim 1, wherein L is phenyl, optionally substituted by halogen up to perhalo.

**10. (Previously Presented)** A compound of claim 1, wherein L is phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of halogen and C<sub>1</sub>-C<sub>3</sub> alkoxy.

**11. (Canceled)**

**12. (Canceled)**

**13. (Canceled)**

**14. (Canceled)**

**15. (Canceled)**

**16. (Canceled)**

**17. (Canceled)**

**18. (Previously Presented)** A compound of claim 4, wherein M is -O- .

**19. (Previously Presented)** A compound of claim 8 wherein M is -O-.

**20. (Previously Presented)** A compound of claim 9 wherein M is -O-.

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21. **(Previously Presented)** A compound of claim 10 wherein M is -O- .
  
22. **(Previously Presented)** A compound of claim 1 wherein L<sup>1</sup> is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, halogen and C<sub>1</sub>-C<sub>6</sub> alkoxy.
  
23. **(Previously Presented)** A compound of claim 3 wherein L<sup>1</sup> is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, halogen and C<sub>1</sub>-C<sub>6</sub> alkoxy.
  
24. **(Previously Presented)** A compound of claim 18 wherein L<sup>1</sup> is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, halogen and C<sub>1</sub>-C<sub>6</sub> alkoxy.
  
25. **(Previously Presented)** A compound of claim 19 wherein L<sup>1</sup> is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, halogen and C<sub>1</sub>-C<sub>6</sub> alkoxy.
  
26. **(Previously Presented)** A compound of claim 20 wherein L<sup>1</sup> is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, halogen and C<sub>1</sub>-C<sub>6</sub> alkoxy.
  
27. **(Previously Presented)** A compound of claim 21 wherein L<sup>1</sup> is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, halogen and C<sub>1</sub>-C<sub>6</sub> alkoxy.

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28. (Canceled)

29. (Canceled)

30. (Canceled)

31. (Canceled)

32. (Canceled)

33. (Previously Presented) A compound of claim 3 wherein  $R_a$  and  $R_b$  are independently hydrogen or  $C_1$ - $C_6$  alkyl.

34. (Previously Presented) A compound of claim 18 wherein  $R_a$  and  $R_b$  are independently hydrogen or  $C_1$ - $C_6$  alkyl.

35. (Previously Presented) A compound of claim 19 wherein  $R_a$  and  $R_b$  are independently hydrogen or  $C_1$ - $C_6$  alkyl.

36. (Previously Presented) A compound of claim 20 wherein  $R_a$  and  $R_b$  are independently hydrogen or  $C_1$ - $C_6$  alkyl.

37. (Previously Presented) A compound of claim 21 wherein  $R_a$  and  $R_b$  are independently hydrogen or  $C_1$ - $C_6$  alkyl.

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**38. (Previously Presented)** A compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is of the formula: -L-M-L<sup>1</sup>, wherein

L is phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of C<sub>1</sub>-C<sub>5</sub> linear or branched alkyl, C<sub>1</sub>-C<sub>5</sub> linear or branched haloalkyl up to perhalo, C<sub>1</sub>-C<sub>3</sub> alkoxy and halogen;

L<sup>1</sup> is pyridinyl, substituted by -C(O)R<sub>x</sub>;

wherein R<sub>x</sub> is NR<sub>a</sub>R<sub>b</sub> and R<sub>a</sub> and R<sub>b</sub> are independently

hydrogen,

C<sub>1</sub>-C<sub>10</sub> alkyl,

C<sub>6</sub> aryl,

pyridinyl, substituted C<sub>1-10</sub> alkyl,

substituted C<sub>6</sub> aryl, or

substituted pyridinyl,

where R<sub>a</sub> and R<sub>b</sub> are a substituted group, they are substituted by halogen up to per halo; and

M is selected from the group consisting of oxygen and sulfur

and

B is phenyl, substituted with 1-3 substituents independently selected from the group consisting of R<sup>7</sup> and halogen;

and R<sup>7</sup> is

(a) C<sub>1</sub>-C<sub>6</sub> linear or branched alkyl, optionally substituted with 1-3 halogen substituents; or

(b) C<sub>1</sub>-C<sub>6</sub> linear or branched alkoxy.

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**39. (Previously Presented)** A compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is of the formula: -L-M-L<sup>1</sup>,

L is phenyl,

M is -O-,

L<sup>1</sup> is pyridinyl substituted by -C(O)R<sub>x</sub>,

wherein R<sub>x</sub> is NR<sub>a</sub>R<sub>b</sub> and R<sub>a</sub> and R<sub>b</sub> are independently hydrogen,

C<sub>1</sub>-C<sub>10</sub> alkyl,

C<sub>6</sub> aryl,

pyridinyl,

substituted C<sub>1-10</sub> alkyl,

substituted C<sub>6</sub> aryl, or

substituted pyridinyl

where R<sub>a</sub> and R<sub>b</sub> are a substituted group, they are substituted by halogen up to per halo, and

B is a phenyl group substituted by trifluoromethyl or tert-butyl, and optionally additional substituents selected from the group consisting of halogen up to per halo, and W<sub>n</sub> where n is 0-3, and each W is independently selected from the group consisting of

C<sub>1</sub>-C<sub>10</sub> alkyl,

C<sub>1</sub>-C<sub>10</sub> alkoxy,

C<sub>6</sub> aryl,

pyridinyl,



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and substituted C<sub>1</sub>-C<sub>10</sub> alkyl, substituted by one or more substituents independently selected from the group consisting of halogen up to per halo.

40. **(Previously Presented)** A compound as in claim 38 wherein the cyclic structures of B and L bound directly to D are substituted in the ortho position by hydrogen.

41. **(Canceled)**

42. **(Previously Presented)** A compound as in claim 39 wherein the cyclic structures of B and L bound directly to D are substituted in the ortho position by hydrogen.

43. **(Canceled)**

44. **(Previously Presented)** A compound as in claim 38 wherein substituents for B, are selected from the group consisting of up to per halo substituted C<sub>1</sub>-C<sub>6</sub> alkyl and halogen.

45. **(Previously Presented)** A compound as in claim 39 wherein the optional substituents for B are selected from the group consisting of up to per halo substituted C<sub>1</sub>-C<sub>6</sub> alkyl and halogen.

46. **(Canceled)**

47. **(Canceled)**

48. **(Canceled)**

49. **(Canceled)**

50. **(Previously Presented)** A pharmaceutically acceptable salt of a compound of formula I of claim 1 which is

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a) a basic salt of an organic acid or inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid; or

b) an acid salt of an organic or inorganic base containing an alkali metal cation, an alkaline earth metal cation, an ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

**51. (Cancelled)**

**52. (Canceled)**

**53. (Previously Presented)** A pharmaceutically acceptable salt of a compound of claim 38 which is

a) a basic salt of an organic acid or inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid; or

b) an acid salt of an organic or inorganic base containing an alkali metal cation, an alkaline earth metal cation, an ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

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**54. (Previously Presented)** A pharmaceutically acceptable salt of a compound of claim 39 which is

a) a basic salt of an organic acid or inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid; or

b) an acid salt of an organic or inorganic base containing an alkali metal cation, an alkaline earth metal cation, an ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

**55. (Previously Presented)** A pharmaceutical composition comprising a compound of claim 1 or a pharmaceutically acceptable salt of a compound of formula I, and a physiologically acceptable carrier.

**56. (Canceled)**

**57. (Canceled)**

**58. (Previously Presented)** A pharmaceutical composition comprising a compound of formula I of claim 38 or a pharmaceutically acceptable salt thereof, and a physiologically acceptable carrier.

**59. (Previously Presented)** A pharmaceutical composition comprising a compound of formula I of claim 39 or a pharmaceutically acceptable salt thereof, and a physiologically acceptable carrier.

**60. (Canceled)**

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**61. (Cancelled)**

**62. (Currently Amended)** A method for inhibiting the enzyme raf kinase in a human or animal, comprising administering a pharmaceutically acceptable amount of a compound of Formula I of claim 1 to said mammal.

**63. (Canceled)**

**64. (Currently Amended)** A method for inhibiting the enzyme raf kinase in a human or animal, comprising administering a pharmaceutically acceptable amount of a compound of Formula I of claim 38 to said mammal.

**65. (Currently Amended)** A method for inhibiting the enzyme raf kinase in a human or animal, comprising administering a pharmaceutically acceptable amount of a compound of Formula I of claim 39 to said mammal.

**66. (Canceled)**

**67. (Canceled)**

**68. (Previously Presented)** A compound of claim 1 wherein the optional substituents on L<sup>1</sup> are selected from the group consisting of methyl, trifluoromethyl, methoxy, Cl and F.

**69. (Previously Presented)** A compound of claim 1 wherein the substituents of B and L are independently selected from the group consisting of methyl, trifluoromethyl, tert-butyl, methoxy, Cl, and F.

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**70. (Currently Amended)** A pharmaceutical composition ~~for the treatment of a cancerous cell growth~~ comprising a compound of formula I of claim 1 or a pharmaceutically acceptable salt of a compound of formula I and a physiologically acceptable carrier.

**71. (Previously Presented)** A compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is  $-\text{NH}-\text{C}(\text{O})-\text{NH}-$ ,

A is a substituted moiety of the formula:  $-\text{L}-\text{M}-\text{L}^1$ ,

wherein L is phenyl, optionally substituted with substituents independently selected from the group consisting of halogen, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>1</sub>-C<sub>5</sub> alkyl substituted by halogen and C<sub>1</sub>-C<sub>5</sub> alkoxy;

L<sup>1</sup> is pyridinyl, substituted with  $-\text{C}(\text{O})\text{NR}^a\text{R}^b$  and optionally substituted with one or two substituents selected from the group consisting of R<sup>7</sup>, OR<sup>7</sup> and halogen, wherein R<sup>7</sup> is hydrogen, C<sub>1</sub>-C<sub>5</sub> alkyl or C<sub>1</sub>-C<sub>5</sub> alkyl substituted by halogen,

wherein R<sup>a</sup> and R<sup>b</sup> independently are

- a) hydrogen or
- b) C<sub>1</sub>-C<sub>5</sub> alkyl;

B is phenyl, substituted by tert-butyl or trifluoromethyl and optionally substituted with additional substituents independently selected from the group consisting of

- a) halogen,
- b) C<sub>1</sub>-C<sub>5</sub> alkyl substituted by halogen or
- c) C<sub>1</sub>-C<sub>4</sub> alkoxy.

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**72. (Currently Amended)** A pharmaceutical composition ~~for the treatment of a cancerous cell growth~~ as in claim ~~71~~ 70 wherein the pharmaceutically acceptable salt is

a) a basic salt of an organic acid or an inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid; or

b) an acid salt of an organic or inorganic base containing an alkali metal cation, an alkaline earth metal cation, an ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

**73. (Canceled)**

**74. (Canceled)**

**75. (Canceled)**

**76. (Canceled)**

**77. (Canceled)**

**78. (Canceled)**

**79. (Canceled)**

**80. (Canceled)**

**81. (Canceled)**

**82. (Canceled)**

**83. (Canceled)**

**84. (Canceled)**

**85. (Canceled)**

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- 86. (Canceled)
- 87. (Canceled)
- 88. (Canceled)
- 89. (Cancelled)